

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
30 June 2005 (30.06.2005)

PCT

(10) International Publication Number  
**WO 2005/058892 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 471/04**,  
A61K 31/437, A61P 29/00, 11/00 // (C07D 471/04,  
231:00, 221:00)

(21) International Application Number:  
PCT/EP2004/014490

(22) International Filing Date:  
17 December 2004 (17.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PCT/EP03/14867

	19 December 2003 (19.12.2003)	EP
0405899.6	16 March 2004 (16.03.2004)	GB
0405936.6	16 March 2004 (16.03.2004)	GB
0406754.2	25 March 2004 (25.03.2004)	GB

(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ALLEN, David, George** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **COE, Diane, Mary** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **COOK, Caroline, Mary** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **DOWLE, Michael, Dennis** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1

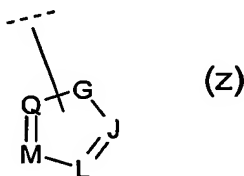
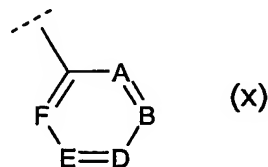
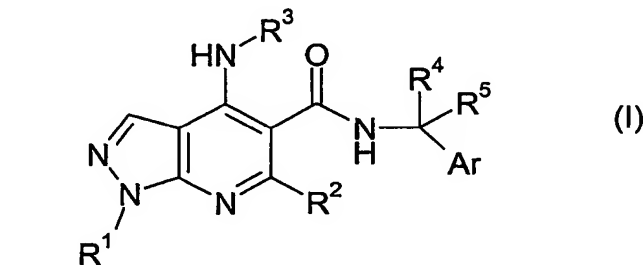
2NY (GB). **EDLIN, Christopher, David** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **HAMBLIN, Julie, Nicole** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **JOHNSON, Martin, Redpath** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **JONES, Paul, Spencer** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **LINDVALL, Mika, Kristian** [FI/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **MITCHELL, Charlotte, Jane** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **REDGRAVE, Allison, Judith** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **ROBINSON, John Edward** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). **TRIVEDI, Naimisha** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB).

(74) Agent: **BREEN, Anthony, Paul**; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: PYRAZOLO [3,4-B] PYRIDINE COMPOUNDS, AND THEIR USE AS PHOSPHODIESTERASE INHIBITORS



(57) Abstract: The invention provides a compound of formula (I) or a salt thereof, wherein Ar has the sub-formula (x) or (z) and wherein R<sup>3</sup> is optionally substituted C<sub>3-8</sub>cycloalkyl, optionally substituted C<sub>5-7</sub>cycloalkenyl, an optionally substituted heterocyclic group (aa), (bb) or (cc), or a bicyclic group (ee); and wherein R<sup>4</sup> is H, C<sub>1-3</sub> alkyl, C<sub>1-2</sub>fluoroalkyl, cyclopropyl, CH<sub>2</sub>OR<sup>4a</sup>, CH(Me)OR<sup>4a</sup>, or CH<sub>2</sub>CH<sub>2</sub>OR<sup>4a</sup>; and R<sup>5</sup> is *inter alia* H, C<sub>1-8</sub>alkyl, C<sub>1-8</sub>fluoroalkyl, C<sub>3-8</sub> cycloalkyl, certain substituted alkyl groups, -(CH<sub>2</sub>)<sub>n</sub><sup>13</sup>- Het, or optionally substituted phenyl or CH<sub>2</sub>-Ph; or R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)p<sup>1-</sup> or (CH<sub>2</sub>)p<sup>3</sup> X<sup>5</sup> (CH<sub>2</sub>)p<sup>4-</sup>; provided that at least one of R<sup>4</sup> and R<sup>5</sup> is not a hydrogen atom (H). The invention also provides the use of the compounds as inhibitors of phosphodiesterase type IV (PDE4) and/or for the treatment and/or prophylaxis of inflammatory and/or allergic diseases such as chronic obstructive pulmonary disease (COPD), asthma, rheumatoid arthritis, allergic rhinitis or atopic dermatitis.



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.